## REMARKS/ARGUMENTS

Explanation of Amendments

Applicants respectfully request entry of the above amendments.

Claims 1, 2, 3, 10 and 65 have been amended. Claims 1-8, 10, 11, 47-50, 61, and 65 are currently pending. The amendments made herein were not made in response to any prior art, and no new matter has been added by way of these amendments.

Applicants note with appreciation the withdrawal of the rejection of claims 6, 8, and 48-50 over Mahairas et al. in view of Sibson et al. in view of the declaration filed 9/17/2004 (The Paszty declaration).

Claim 8 is objected to under 37 CFR §1.75(c) as being in alleged improper form because a multiple dependent claim can depend from multiple other claims in the alternative only. Claim 8 is said to depend from claims 1, 2 or 3, and claim 8. Applicants are unclear as to how claim 8 is said to depend from claim 8. According to Applicants' records claim 8 reads as follows:

> 8. A process of producing a polypeptide encoded by the nucleic acid molecule of Claims 1, 2, or 3 comprising culturing the host cell of Claim 5 under suitable conditions to express the polypeptide, and optionally isolating the polypeptide from the culture.

Clarification is requested.

Claims 1-8, 10, 11, 47-51, 61 and 65 are rejected under 35 U.S.C. §112, second paragraph, as being allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, the Office action states that claims which recite specific stringent conditions, such as claims 1-3, are said to remain indefinite because the metes and bounds of what will be obtained by such hybridization are believed to be as dependent upon the wash conditions (time and buffers) as they are upon the actual hybridization conditions. In response thereto, Applicants have added a limitation into the relevant claims, specifically reciting a wash step following the hybridization step. No new matter has been added by way of this amendment. Support for a wash step can be found at, e.g., page 31, lines 20-33. Withdrawal of this rejection is respectfully requested.

Claim 2 (part d) and claim 3 (part f) as amended are said to be indefinite for referring inclusively to previous parts of the claims. Claims 2 and 3 have been amended accordingly. Withdrawal of this rejection is requested.

Claim 3 is said to remain indefinite for allegedly failing to adequately point out that which Applicant sees as the invention. The Office Action states that there is no upper limit to the number of substitutions, insertions, deletions, or truncations, such that there is no requirement for any structural similarity to the disclosed nucleic acids.

In response thereto, claim 3 has been amended to recite at least about 90% identity to a mature form of the polypeptide. The full-length form is set forth in SEQ ID NO: 1, and the predicted mature form is set forth in SEQ ID NO: 3. No new matter has been added by way of this amendment. Support can be found at, e.g., page 34, lines 16-31 of the specification.

Claim 10 is said to be indefinite as there is no antecedent basis for "the B10 polypeptide" in any of the claims form which it depends, in view of the prior amendments to the claims. In response thereto, Applicants have removed reference to the β10 polypeptide from claim 10. Applicants respectfully request withdrawal of this rejection.

Claim 65 is said to be indefinite for depending from a cancelled claim. Claim 65 has been amended to properly depend from claim 5, which recites the host cell.

Claims 1-8, 10, 11, 47-51, 61 and 65 remain rejected under 35 U.S.C. §112, first paragraph. The Office Action states that the specification, while being enabling for a nucleic acid of SEQ ID NO: 2 or one that encodes SEQ ID NO: 1, does not reasonably provide enablement for the breadth of the claims, which encompass fragments, derivatives, etc. of such. The specification is said not to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

In support thereof, the Office Action recites the *Wands* factors. Applicants have considered the arguments in the Office Action, and in response thereto have now amended the relevant claims to recite only those polypeptides that are at least about 90% identical to a mature form of the polypeptide, as set forth in SEQ ID NO: 3. As noted by the Office Action, Applicants discovered two new glycoprotein hormone subunits, α2 and β10. While the claims should necessarily be commensurate with the scope of Applicant's discovery, they should similarly not be unduly restricted. To

narrow Applicants' claims strictly to the exact nucleotide and amino acid sequences would be to unduly narrow the claims, and would only invite infringement by third parties. Applicants believe that restriction of the claims to polypeptides having at least about 90% identity is a reasonable balance of these considerations.

Claims 1-8, 10, 11, 47-51, 61 and 65 remain rejected under 35 U.S.C. §112, 1st paragraph. The Office Action asserts that the claims contain subject matter not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention for reasons of record in the first office action on the merits, mailed 11/21/2002. Specifically, the Office Action states that the previous recitation of 75% identity is inadequate because such variation is not limited to that in the non-coding regions of SEQ ID NO: 1. Applicants have now amended the claims to recite about 90% identity to a mature form of the polypeptide as noted above.

Applicants believe it would be unduly restrictive to limit the claims strictly to SEQ ID NO:1, or SEQ ID NO: 3. It is known in the art that certain minor amino acid changes can still result in retained activity in the instant polypeptide(s), and these are contemplated by the present invention. To restrict the claims in this way would be to invite infringement by third parties who could make minor changes in Applicants' sequences, while retaining the specified activity, but would avoid infringement due to this undue narrowing of the claims. Applicants respectfully request reconsideration.

Claims 2, 4-5, 7, and 11 remain rejected under 35 U.S.C. §102(b) as being allegedly anticipated by, or in the alternative under 35 U.S.C. §103(a) as being allegedly obvious over G.G. Mahairas *et al.*, Locus AQ495547.

As noted previously, a reference cited under 35 U.S.C. §102, must singly identify each and every feature recited in the claim it is asserted against. *Scripps Clinic and Research Foundation v. Genentech, Inc.*, 927 F.2d 1565, 1576 (Fed. Cir. 1991); *Verdegaal Bros. v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Additionally, for a reference to be effective under 35 U.S.C. §102, that reference must contain an enabling disclosure. See *In re Hoeksma*, 399 F.2d 269, 158 USPQ 596 (CCPA 1968); *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1354, 65 USPQ2d 1385, 1416 (Fed. Cir. 2003).

As also noted previously, the reference must enable one of skill in the art to both make and use the claimed invention. *See PPG Industries, Inc. v. Guardian Industries Corp.*, 75 F.3d 1558, 1566, 37 USPQ2d 1618, 1624 (Fed. Cir. 1996).

Mahairas describes a BAC clone containing a piece of human genomic DNA. Nothing more. The sequence is completely unannotated, identifies no reading frame, no cloning orientation (5' or 3'), no introns, exons, genes, or homologies to other molecules. As also noted previously, cysteines C12, C36, and C40 (which are critical the activity of the molecule), are not present in the truncated β10 polypeptide present in Mahairas.

The Office Action here simply asserts that:

> "Applicants traversal... has been fully considered but is not deemed persuasive."

No support for this assertion is provided. The Patent and Trademark Office bears the burden of supporting its rejections, and the nature of those rejections must be stated with particularity. *See* MPEP §707.07(D). Clarification of the basis for rejecting Applicants' arguments is respectfully requested.

In an effort to expedite prosecution, however, Applicants have amended the claims to recite about 90% identity to a mature form of the polypeptide. Applicants note that the genomic sequence recited in Mahairas, however translated, would at best result in a truncated sequence of approximately 58% identity to a mature form of SEQ ID NO: 1 (as shown in SEQ ID NO: 3) *nowhere near* the about 90% identity now claimed by Applicants. Withdrawal of this rejection is requested.

Claims 2, 4-5, 7, and 11 remain rejected under 35 U.S.C. §103(a) as being allegedly obvious over G.G. Mahairas *et al.*, Locus AQ495547. Although the Office Action does not recite any other references as the basis for the rejection, Applicants assume this rejection includes the previously-cited Sibson *et al.* reference, WO 94/01548.

Sibson *et al.* appears to teach the use of a desired cDNA sequence in an expression vector and host cell, and subsequent expression of the encoded protein, and raising antibodies to proteins encoded by such DNAs.

To reiterate, Mahairas describes incomplete, genomic DNA, with an intron, no reading frame or orientation, no utility, and corresponds to an *inactive* portion of the β10 molecule. This molecule would not fold properly and would lack biologic activity.

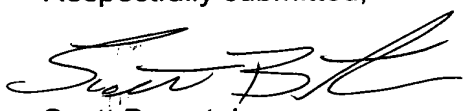
As noted above, Applicants have amended the claims to recite about 90% identity to a mature form of the polypeptide, and the genomic sequence recited in Mahairas, however translated, is far from the about 90% identity now claimed by Applicants.

Sibson relates to completely unrelated cDNA sequences (*i.e.*, *not* genomic DNA), and methods of producing the same. There is no suggestion in the cited references to combine Mahairas and Sibson. And even if one skilled in the art were motivated to combine these references (Applicants maintain they would not) the combination of

Mahairas and Sibson would result in a misfolded, inactive peptide fragment that is not about 90% identical to Applicants claimed sequences.

In view of the above, withdrawal of this rejection is respectfully requested.

Respectfully submitted,



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